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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,710	11/08/2001	Aristo Vojdani	IMSC12.004A	7714
20995	7590	05/26/2004	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			NGUYEN, BAO THUY L	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/005,710	VOJDANI, ARISTO	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Election/Restrictions*

1. This application contains claims directed to the following patentably distinct species of the claimed invention: myosin, oxidized LDL, heat shock protein-60,  $\beta$ -2-glycoprotein-1, platelet glycoprotein, and immune complexes, species 1-6 respectively.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 3-6 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

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During a telephone conversation with Daniel Altman on May 19, 2004 a provisional election was made with traverse to prosecute the invention of species 2 (oxidized LDL).

Affirmation of this election must be made by applicant in replying to this Office action.

*Amendment*

2. Applicant's preliminary amendment filed on July 02, 2002 has been received. Claims 1-6 are pending.

*Information Disclosure Statement*

3. Some of the references included in the information disclosure statement filed on March 15, 2001 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because they are not legible.

*Claim Rejections - 35 USC § 112, first paragraph*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting antibodies against certain auto antigens and for indicating the presence or possibility of cardiovascular disease, does not reasonably provide enablement for a method for diagnosing the severity of cardiovascular disease, nor is it enabling for a prediction of early pathogenic reaction for a cardiovascular disease. The specification does

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not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches the detection of salivary IgA against several auto antigens that are alleged to be related to cardiovascular diseases. Any elevation in the level of IgA in patients' samples as compared to normal control subjects indicates possible cardiovascular disease. Nowhere in the specification is there a teaching of a method for diagnosing the severity of a cardiovascular disease or a method for prediction of early pathogenic reaction for a cardiovascular disease.

According to Strongin (1993, "Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications", in Laboratory Diagnosis of Viral Infections, Lennette, e., ed., Marcel Dekker, Inc., New York, pp. 211-219) a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the following: (1) the sensitivity of the assay; (2) the true-positive test rate; (3) the false-negative test rate; (4) the specificity, or percentage of patients without the disease who will display a negative results; (5) the true-negative test rate; (6) the false-positive test rate; (7) the predictive value, or the probability that the test result is correctly indicating the presence or absence of the disease; (8) the prevalence, or number of patients in any given population that have the disease in question; (9) the efficiency or percentage of all results that are true; (10) the accuracy of the recited diagnostic assay. Additional considerations must also be examined to enable the clinician to practice the invention including assessment of the following: (1) when is the maximum sensitivity desired? (2) when is the maximum specificity desired?; (3) when is the maximum efficiency desired?; (4) How is the maximum sensitivity or specificity achieved?; (5)

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how is the predictive value maximized? An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test.

Since the specification lacks any teaching of a method for diagnosing the severity of a cardiovascular disease or a method for prediction of early pathogenic reaction for a cardiovascular disease, or any information regarding the patients from which the samples were taken, and whether any considerations were given to any of the characteristics state above, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Because of the lack of description in the specification for the claimed method, the data presented in tables 2 and 3 and the examples do not allow the conclusive determination that anyone or everyone who has an elevated level of IgA to oxidized LDL has a certain severity of cardiovascular disease. The specification also does not enable one skilled in the art to use these data in a method for predicting early pathogenic reaction for a cardiovascular disease.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

6. Claims 1 and 3-6 are further rejected because the specification is not enabling for a method of detecting antibodies against any and all auto antigens. Specifically, the specification discloses the detection of IgA against oxidized LDL, comparing the detected level to those of normal control subjects and any elevation in the level of IgA is diagnostic for a possibility of cardiovascular disease. The specification at pages 3-8 teaches that the development of autoimmunity to myocardial antigens, for example, has been recognized after myocardial infarction or after cardiac surgery. Furthermore, the specification discloses that oxidized LDL autoantibodies have been detected in the bloodstream of patients with coronary artery disease,

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etc. Nowhere in the specification is there a disclosure of any other autoantigens, other than myosin, oxidized LDL, heat shock protein-60,  $\beta$ -2-glycoprotein-1, platelet glycoprotein, and certain immune complexes, as being diagnostic for cardiovascular disease.

*Claim Rejections - 35 USC § 112, second paragraph*

7. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing because the preamble of the claim does not correlate with the analysis of the detected result. For example, the preamble recites a method for diagnosing the likelihood and severity of cardiovascular disease; however, the detected result is recited as indicating ongoing pathology or prediction of early pathogenic reaction for cardiovascular disease.

Claim 1 is also vague and indefinite because it is a method for diagnosing the likelihood of cardiovascular disease in a patient using a sample from said patient. However, claim 1 recites that the method involves the determination of antibodies against a recombinant antigen or synthetic peptide in said sample. This is confusing since recombinant antigen and synthetic peptide are not generally present in a patient sample. Therefore, it is unclear how antibodies may exist against such antigens.

Claim 2 is vague and indefinite because it is unclear what kind of immune complexes are being detected or how these unknown immune complexes can be correlated to cardiovascular disease.

### *Double Patenting*

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/005,684. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are claiming a method for diagnosing a disease by detecting the level of IgA, for example, against an auto antigen such as immune complexes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 102*

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**10.** Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Kovanen et al (*Archives of Internal Medicine*. July 13, 1998. Vol. 158, No. 13, pages 1434-1439, IDS).

Kovanen discloses elevated levels of IgA, IgE and IgG in patients with established arteriosclerosis and myocardial infarction or cardiac death. See page 1435. Kovanen discloses autoantigens and several exogenous antigens as having been implicated in the pathogenesis of myocardial infarction including oxidized LDL and cardiolipin. See page 1437.

#### *Claim Rejections - 35 USC § 103*

**11.** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**12.** Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovanen in view of Stone et al., (*Journal of Human Stress*. 1987. Vol. 13, pages 136-140).

See the discussion of Kovanen above. This reference differs from the instant invention in failing to teach the detection of IgA in saliva.

Stone, however, teaches the measurement of IgA antibody response to a particular antigen in saliva using ELISA. Stone teaches that although IgA is also present in serum, secretory IgA (sIgA) is more advantageous in that it is much larger and binds invading

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organisms more effectively than serum IgA. Stone also teaches that sIgA can be collected rather simply and inexpensively in saliva and quantitated with a readily available assay. See page 138.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Kovanen to measure sIgA and relating the measured level with diseases such as cardiovascular disease because Stone teaches that sIgA can be measured with ease and the level of sIgA can be directly correlated with immunocompetence. The collection of samples such as saliva is simple and painless and the measurement of sIgA against a specific antigen provides the advantage of a method that has few problems and provides a more meaningful assessment of the sIgA system.

### *Conclusion*

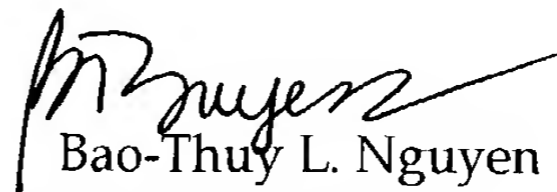
**13.** No claim is allowed.

**14.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 9:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Bao-Thuy L. Nguyen  
Primary Examiner  
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